REMARKS

Claims 1 to 11 are pending.

The rejection of claims 1 to 11 under 35 U.S.C. § 112, second paragraph, as allegedly vague and indefinite respectfully is traversed.

It is stated in the Office Action that the claims 1 5o 3, 5 and 7 to 11 recited methods of treating a cell proliferative disorder "associated with expression" of 5'ALT or p16 with a "reagent", but that the there is no specific disease recited in the claims and no specific structural characteristics of the reagent or specific methods of administration. It is stated, for example, that the claims can read on administration of a "poison", which can inhibit gene expression and, therefore, are not clear as to the boundary between effective and non-effective reagents.

Although it can be argued that the claims can read on administration of a "poison," the predecessor to the Federal Circuit, in addressing an enablement matter, recognized that methods of treatment involve "a highly technical subject in an art requiring a high degree of technical skill - doctors of medicine and pharmacologists [and] that some medicines of great utility are lethal when used in the wrong quantity...." In re Anderson 176 U.S.P.Q. 331, 334 (CCPA 1973). The court went on to state that the use of a medication is "inherently limited - by common sense if nothing else - to such medication as would be useful in the particular application. No one of ordinary skill in the art would use any other kind of medicament and there is no practical way to restrict the claim language as to exclude all inoperative or deleterious medicaments...." Id. at pages 334-335. By analogy, it is submitted that one skilled in the art, reading the claims, clearly would be apprised, if only by "common sense", that a "reagent" useful in a method of the invention would not encompass non-specific poisons. Accordingly, it is respectfully requested

Further with regard to reagents that can be useful in a method of the invention, the specification discloses (and the claims recite) that an antibody (claim 4) or a polynucleotide (claim 5) such as an antisense sequence (claim 6) can be used as such reagents. The specification also discloses triplexing agent and ribozymes as additional examples of polynucleotides useful in a method of the invention (see, for example, page 33, second full paragraph, to page 34, second paragraph). In addition, the specification discloses (and the claims recite) that a drug such as a demethylating agent (claim 10), for example, 5'-deoxyazacytidine (claim 11), can be used where the disorder is associated with methylation of a CpG island of a p16 gene. As such, the specification discloses "reagents" as diverse as polynucleotides, polypeptides, and small organic molecules, which can be used in a method of the invention.

With respect to the disorders encompassed within the claims, Applicants maintain that one skilled in the art would know, in view of the claims and the specification, that a cell proliferative disorder associated with expression of a 5' ALT polynucleotide would encompass those disorders, first, in which the level of 5' ALT as compared to a corresponding normal cell (see, for example, page 31, second full paragraph), and second, where cell proliferation is altered with respect to a corresponding normal cell. As such, in view of the specification, it is submitted that one skilled in the art clearly would be apprised of those disorders encompassed within the claims and, therefore, amenable to treatment using a method of the invention.

In summary, it is submitted that amended claims 1 to 11 clearly define the subject matter regarded as the invention such that one skilled in the art, viewing the claims and the specification, would know the metes and bounds of the claimed invention. Accordingly, it is respectfully requested that the rejection of claims 1 to 11 under 35 U.S.C. § 112, second

The objection to the specification and corresponding rejection of claims 1 to 11 under 35 U.S.C. § 112, first paragraph, as allegedly containing lacking enablement respectfully are traversed.

It is maintained in the Office Action, for the reasons of record, that the specification does not disclose how one readily identifies a cell proliferative disorder associated with 5'ALT and with p-16, or how to predictably treat such disorders using various methods, including gene therapy. In response to Applicants' previous argument that the specification clearly teaches one skilled in the art how to identify a cell proliferative disorder amenable to treatment, it is stated in the present Office Action that the claims are not directed merely to methods of identifying abnormal gene expression patterns associated with such cell proliferative disorders, but to the treatment of such disorders. Applicants point out, however, that the previous arguments were in response to the allegation in the Office Action dated June 22, 2000, where it was stated that the specification does not teach identifying such disorders (see Paper No. 3, page 3). As such, Applicants merely were responding to one of the issues raised in the Office Action.

In the previous response, Applicants further pointed out various disclosures in the specification that teach how to use reagents such as a polynucleotide for a gene therapy procedure, or using an antibody that binds to a polypeptide encoded by a 5'ALT polynucleotide (see, for example, amended claim 4), or using a demethlyating agent such as 5'-deoxyazacytidine (see paragraph bridging pages 32 to 33; page 43, lines 8-11; see, also, claims 10 and 11). More specifically, Applicants pointed to the Stolberg article, which was cited in the Office Action mailed June 22, 2000, as reporting that clinical trials of gene-based treatments for hemophilia are showing promise, and certain cancer patients appear to respond to gene therapy.

In the present Office Action, it is argued that all of the positive results specific treatments as described by Stolberg were directed to specific diseases after determining that the disorder was associated with the absence of a gene product. Applicants point out, however, that the present claims are directed to treatment of cell proliferative disorders "associated with expression of a 5' ALT polynucleotide" (claims 1 to 8) or "associated with altered p16 expression due to methylation" (claims 9 to 11). Thus, the present claims are directed to methods of treating a disorder that is characterized by altered expression of a specific gene, similar to the disorders treated by gene therapy as described by Stolberg. As such, it is submitted that, in view of the Stolberg reference, which discloses that gene therapy can be effective for treating a disorder associated with aberrant expression of a specific gene, one skilled in the art, viewing the specification, would have known that a gene therapy method reasonably would be expected to be useful for treating a cell proliferative disorder associated with expression of a 5' ALT polynucleotide (claims 1 to 8). Furthermore, it is submitted that one skilled in the art, viewing the specification, would have known that a demethylating agent such as 5'-deoxyazacytidine can be used to treat a cell proliferative disorder associated with altered p16 expression due to methylation of a CpG island of a p16 gene.

As further evidence that the specification would have enabled one skilled in the art to practice a method of the invention as claimed, Applicants have submitted herewith the Liggett et al. reference (Cancer Res. 56:4119-4123, 1996; attached as Exhibit A), which was published after the June 30, 1995, priority date of the subject application. Liggett et al. describe, for example, that introduction of a polynucleotide encoding p16β (i.e., the 5'-ALT polynucleotide) into cells of a head and neck squamous cell carcinoma (HNSCC) cell line or into HeLa cells resulted in growth inhibition of the tumor cells (see Exhibit A; Abstract). It is noted that the

Thus, the Liggett et al. reference demonstrates that introduction of a 5' ALT polynucleotide into a tumor cell can inhibit the growth of the tumor cells and, therefore, provides confirmatory evidence that, as disclosed in the specification, a reagent that modulates 5' ALT expression or activity in a cell can treat a cell proliferative disorder. Applicants point out that the Liggett et al. reference is being submitted only to confirm that the specification as filed would have enabled one skilled in the art to practice the claimed methods (see Gould v. Quigg, 3 U.S.P.Q.2d 1302 (Fed. Cir. 1987); later dated publication can be used as evidence that the disclosed invention was operative, Id. at page 1305).

In summary, it is submitted that one skilled in the art, viewing the specification, would have known that a cell proliferative disorder such as a neoplasm associated with expression of a 5' ALT polynucleotide can be treated using a method of the invention, would have known how to identify other such disorders amenable to treatment according to a method of the invention, and would have known that a method such as a gene therapy method or a method using an antibody can be used to effectively treat such as disorder. The Liggett et al. reference submitted herewith provides confirmatory evidence that a method such as a gene therapy method can effectively treat such a cell proliferative disorder, as disclosed in the specification. Accordingly, it is respectfully requested that the objection to the specification be withdrawn and that the corresponding rejection of claims 1 to 11 under 35 U.S.C. § 112, first paragraph, be removed.

In view of the above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect respectfully is requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

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Enclosure: Exhibit A